

What is claimed is:

1. A high molecular weight aptamer composition comprising:
  - (a) a nucleic acid comprising two or more aptamers, and
  - (b) a stabilizing moiety comprising a linking moiety, wherein the linking moiety is not a nucleic acid molecule.
2. The aptamer composition of claim 1, wherein the linking moiety comprises a polyalkylene glycol.
3. The aptamer composition of claim 2, wherein the linking moiety comprises polyethylene glycol (PEG).
4. The aptamer composition of claim 3, wherein the nucleic acid comprises first and second aptamers.
5. The aptamer composition of claim 4, wherein the first and second aptamers are linked by the PEG linking moiety, and further wherein the primary structure of the aptamer composition comprises a linear arrangement in which the first aptamer is linked to a first terminus of the PEG linking moiety and the second aptamer is linked to a second terminus of the PEG linking moiety.
6. The aptamer composition of claim 3, wherein the polyethylene glycol (PEG) linking moiety is multi-activated.
7. The aptamer composition of claim 6, wherein the PEG linking moiety is bi-activated.
8. The aptamer composition of claim 1, wherein the aptamer composition is capable of binding to platelet derived growth factor (PDGF).
9. The aptamer composition of claim 1, wherein the aptamer composition is capable of binding to TGF $\beta$ 2.

10. The aptamer composition of claim 1, wherein the high molecular weight aptamer composition has a molecular weight selected from the group consisting of greater than 10 kD, greater than 20 kD, greater than 40 kD and greater than 80 kD.
11. A high molecular weight aptamer composition comprising:
  - (a) a nucleic acid moiety comprising two or more aptamer domains joined by a linker domain, and
  - (b) a stabilizing moiety comprising one or more polyalkylene glycol moieties attached to the linker domain.
12. The aptamer composition of claim 11, wherein the stabilizing moiety comprises one or more polyethylene glycol (PEG) moieties.
13. The aptamer composition of claim 11, wherein the aptamer composition is capable of binding to platelet derived growth factor (PDGF).
14. The aptamer composition of claim 11, wherein the aptamer composition is capable of binding to TGF $\beta$ 2.
15. The aptamer composition of claim 11, wherein the high molecular weight aptamer composition has a molecular weight selected from the group consisting of greater than 10 kD, greater than 20 kD, greater than 40 kD and greater than 80 kD.
16. A high molecular weight aptamer composition comprising:
  - (a) a nucleic acid comprising two or more aptamer domains and a linker domain, and
  - (b) a stabilizing moiety comprising an oligonucleotide splint which hybridizes to at least a portion of the linker domain, wherein the oligonucleotide splint comprises a nucleotide sequence having at least 40 nucleotides.
17. The aptamer composition of claim 16, wherein the oligonucleotide splint hybridizes to at least 20 nucleotides of the linker domain.

18. The aptamer composition of claim 16, wherein the aptamer composition is capable of binding to platelet derived growth factor (PDGF).
19. The aptamer composition of claim 16, wherein the aptamer composition is capable of binding to TGF $\beta$ 2.
20. The aptamer composition of claim 16, wherein the high molecular weight aptamer composition has a molecular weight selected from the group consisting of greater than 10 kD, greater than 20 kD, greater than 40 kD and greater than 80 kD.
21. A high molecular weight aptamer composition comprising:
  - (a) a nucleic acid moiety comprising two or more aptamer domains and a linker domain, and
  - (b) a stabilizing moiety comprising an oligonucleotide splint that hybridizes to at least a portion of the linker domain, wherein the oligonucleotide splint has one or more polyalkylene glycol moieties attached thereto.
22. The aptamer composition of claim 16, wherein the oligonucleotide splint hybridizes to at least 20 nucleotides of the linker domain.
23. The aptamer composition of claim 21, wherein the oligonucleotide splint has one or more polyethylene glycol (PEG) moieties attached thereto.
24. The aptamer composition of claim 21, wherein the oligonucleotide splint comprises a nucleotide sequence having at least 40 nucleotides.
25. The aptamer composition of claim 21, wherein the aptamer composition is capable of binding to platelet derived growth factor (PDGF).
26. The aptamer composition of claim 21, wherein the aptamer composition is capable of binding to TGF $\beta$ 2.

27. The aptamer composition of claim 21, wherein the high molecular weight aptamer composition has a molecular weight selected from the group consisting of greater than 10 kD, greater than 20 kD, greater than 40 kD and greater than 80 kD.
28. A high molecular weight aptamer composition comprising:
- (a) a nucleic acid moiety comprising two or more aptamer domains and a linker domain, and
  - (b) a stabilizing moiety comprising an oligonucleotide splint which hybridizes to at least a portion of the linker domain,
- wherein at least one of the two or more aptamer domains is in the unbound state.
29. The aptamer composition of claim 28, wherein the oligonucleotide splint hybridizes to at least 20 nucleotides of the linker domain.
30. The aptamer composition of claim 28, wherein the oligonucleotide splint comprises a nucleotide sequence having at least 40 nucleotides.
31. The aptamer composition of claim 30, wherein the oligonucleotide splint has one or more polyalkylene glycol moieties attached thereto.
32. The aptamer composition of claim 31, wherein the oligonucleotide splint has one or more polyethylene glycol (PEG) moieties attached thereto.
33. The aptamer composition of claim 28, wherein the aptamer composition is capable of binding to platelet derived growth factor (PDGF).
34. The aptamer composition of claim 28; wherein the aptamer composition is capable of binding to TGF $\beta$ 2.
35. The aptamer composition of claim 28, wherein the high molecular weight aptamer composition has a molecular weight selected from the group consisting of greater than 10 kD, greater than 20 kD, greater than 40 kD and greater than 80 kD.

36. A therapeutic composition comprising the aptamer composition of claim 1.
37. A therapeutic composition comprising the aptamer composition of claim 11.
38. A therapeutic composition comprising the aptamer composition of claim 16.
39. A therapeutic composition comprising the aptamer composition of claim 21.
40. A therapeutic composition comprising the aptamer composition of claim 28.
41. A high molecular weight aptamer composition comprising:
  - (a) an aptamer, and
  - (b) two or more non-nucleic acid stabilizing moieties.
42. The aptamer composition of claim 41, wherein the stabilizing moieties comprise a polyalkylene glycol.
43. The aptamer composition of claim 42, wherein the stabilizing moieties comprise polyethylene glycol (PEG).
44. The aptamer composition of claim 41, wherein the aptamer is multi-activated.
45. The aptamer composition of claim 44, wherein the aptamer is bi-activated.
46. A method of improving the pharmacokinetic or pharmacodynamic properties of an aptamer therapeutic composition comprising the steps of introducing reactive groups in a nucleic acid aptamer, reacting the reactive groups on the aptamer with reactive groups on a stabilizing moiety, thereby forming a stabilized high molecular weight therapeutic aptamer.
47. The method of claim 46 wherein the reactive groups on the aptamer composition are amino groups at 5' or 3' ends of the aptamer introduced by modified phosphoramidite synthesis.

48. The method of claim 46 wherein the stabilizing moiety is polyethylene glycol (PEG).
49. The method of claim 48 wherein the PEG is homo-bifunctional and the resulting aptamer is a dimer linked by a PEG linker.
50. The method of claim 46 wherein the aptamer is multiply activated.
51. The method of claim 50 wherein the aptamer is bi-activated at 5' and 3' termini.
52. The method of claim 50 wherein the stabilizing moiety is a mono-activated PEG and the resulting aptamer is bi-PEGylated.
53. A method of treating disease in a subject comprising the steps of administering a therapeutically effective amount of a high molecular weight aptamer composition of claim 1.
54. A method of treating disease in a subject comprising the steps of administering a therapeutically effective amount of a high molecular weight aptamer composition of claim 11.
55. A method of treating disease in a subject comprising the steps of administering a therapeutically effective amount of a high molecular weight aptamer composition of claim 16.
56. A method of treating disease in a subject comprising the steps of administering a therapeutically effective amount of a high molecular weight aptamer composition of claim 21.
57. A method of treating disease in a subject comprising the steps of administering a therapeutically effective amount of a high molecular weight aptamer composition of claim 28.